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Patricia A. Kammerer			EXAMINER		
Howrey Simon 750 Bering Dri	Arnold & White, LLP ve		DIBRINO, MAF	RIANNE NMN	
Houston, TX 77057-2198		•	ART UNIT	PAPER NUMBER	
			1644	7	
			DATE MAILED: 07/28/2003		
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Please find below and/or attached an Office communication concerning this application or proceeding.

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Applicant(s) Application No. UNION ET AL. 09/747.029 Office Action Summary Art Unit Examiner 1644 DiBrino Marianne

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.

 Failur Any re 	e to reply within the set or extended period for rep	Iv will, by s	ariod will apply and will expire SIX (6) MONTHS from the mailing date of this communication. tatute, cause the application to become ABANDONED (35 U.S.C. § 133). nailing date of this communication, even if timely filed, may reduce any				
Status	o patorit toriii aajasiintorii. Good oo ar ii iiro ii oji						
1)⊠	Responsive to communication(s)	filed on	<u>02 December 2002 and 18 April 2003</u> .				
2a) <u></u> □	This action is FINAL .	2b)⊠	This action is non-final.				
3) [3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213. Disposition of Claims						
•		27 in/ord	a nonding in the application				
	Claim(s) <u>1-9,12-15,18,20 and 23-</u>						
	4a) Of the above claim(s) <u>23</u> is/are	withura	will from consideration.				
-	Claim(s) is/are allowed.	7'-/	and and all				
•	Claim(s) <u>1-9,12-15,18,20 and 24-2</u>	<u>7</u> is/are	rejected.				
	Claim(s) is/are objected to.						
,	Claim(s) are subject to rest	riction a	nd/or election requirement.				
	on Papers	h . 					
·—	The specification is objected to by t						
10)[1	* ' '		accepted or b) objected to by the Examiner.				
			to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).				
11) ☐ The proposed drawing correction filed on is: a) ☐ approved b) ☐ disapproved by the Examiner.							
If approved, corrected drawings are required in reply to this Office action.							
,—	The oath or declaration is objected	to by the	e Examiner.				
•	nder 35 U.S.C. §§ 119 and 120						
13)⊠	Acknowledgment is made of a clai	m for fo	reign priority under 35 U.S.C. § 119(a)-(d) or (f).				
a)[☑ All b)☐ Some * c)☐ None of	•					
	1.⊠ Certified copies of the priorit	y docun	nents have been received.				
	2. Certified copies of the priorit	y docun	nents have been received in Application No				
	application from the Inte	rnationa	priority documents have been received in this National Stage all Bureau (PCT Rule 17.2(a)). a list of the certified copies not received.				
14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).							
a) ☐ The translation of the foreign l	anguage	e provisional application has been received.				
15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.							

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 20

4) Interview Summary (PTO-413) Paper No(s).

Notice of Informal Patent Application (PTO-152)

Attachment(s)



1. Applicant's amendments filed 12/2/02 (Paper No. 19) and 4/18/03 (Paper No. 22) are acknowledged and have been entered.

2. The numbering of claims is not accordance with 37 C.F.R. 1.126. The original numbering of the claims must be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When claims are added, except when presented in accordance with 37 CFR 1.121(b), they must be renumbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

In the present instance, Applicant has presented two new claims numbered "25" in Applicant's marked-up copy of the amendment filed 4/18/03. The first of the said two new claims has been renumbered "24".

3. Applicant is reminded of Applicant's election of Group X (claims 1-9, 12-15 and 18-22), drawn to a cyclic peptide comprising the primary amino acid structure consisting of SEQ ID NO: 4, a composition thereof, and immunotoxin comprising said peptide, and composition thereof, and kit comprising said peptide, and species of SEQ ID NO: 12 in Paper No.17.

Applicant is reminded that upon consideration of a search of the prior art, since SEQ ID NO: 4 and 12 appear to be free of the prior art, the search has been extended to include the peptides taught by the prior art references cited below in this action.

4. Newly submitted claim 23 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claim 23 is drawn to a method for detecting antibodies present in sera from patients with RA using a peptide, classified in Class 435, subclass 7.1, whereas the instant claims of elected Group X are drawn to a cyclic peptide/composition thereof, and immunotoxin comprising said peptide, and composition thereof, and kit comprising said peptide, classified in Class 530, subclasses 317, 345 and 402 and Class 435, subclass 975.

The invention of Group X and that of claim 23 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)).

In the instant case, the product as claimed can be used in a materially different process such as immunopurification procedures or as an immunogen.



Therefore, they are patentably distinct.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 23 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP §

Claims 1-9, 12-15, 18, 20 and 24-27 are currently being examined.

The following are new grounds of rejection necessitated by Applicant's amendment filed 12/2/02.

- 5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
- 6. Claims 1-9, 12-15, 18, 20 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not disclosed in the specification and claims as originally filed is as follows: "a peptide comprising a sequence of 14-50 amino acid residues" recited in claim 1. Applicant does not point to support for the amendatory material. The instant specification discloses a peptide comprising a sequence of *less than* 50 amino acid residues.

7. Claims 1-9, 12-15, 18, 20 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the...claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention

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of the claimed: A peptide comprising/having a sequence of 14-50 amino acids characterized by the recited elements of the instant claims, composition thereof, and immunotoxin comprising said peptide, and composition thereof, and kit comprising said peptide.

The instant claims encompass minimally a peptide that is 14-50 amino acid residues in length, and the open transitional phrases comprising/comprises/has encompass peptides longer than 50 amino acid residues. There is insufficient disclosure in the specification on peptides of 19 and 50 amino acid residues in length and longer that conform to the limitations recited in instant claim 1 as well as the other instant claims.

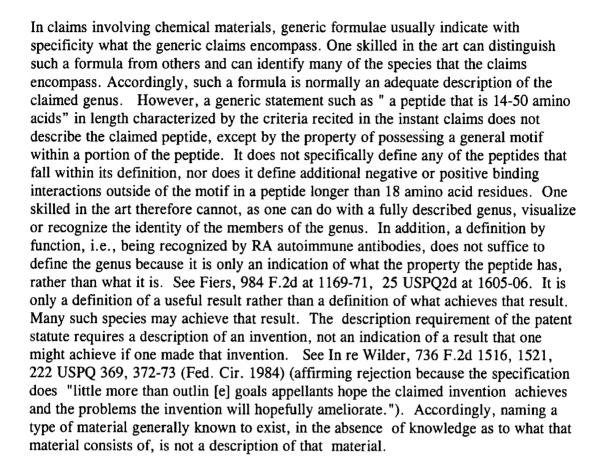
The specification discloses peptides of the invention are less than 50 amino acids and contain a peptide turn comprising at least one citrulline residue, less than 12 amino acid residues between two cysteine residues with said citrulline residue being one of the amino acids between the said cysteine residues and the said peptides being specifically recognized by autoimmune antibodies from patients suffering from RA (page 5 at lines 13-19). The specification discloses that the peptides have a length of preferably 40, 30, 25, 20 or less amino acids (page 7 at lines 23-26). The specification further discloses that the said peptides have a length between 13 and 19 amino acids (page 10 at lines 9-11). The specification discloses peptides with motifs 18 amino acids or less in length recited in instant claim 7, and peptides with complete sequences of 18 amino acids or less in length recited in instant claim 9.

The specification does not disclose peptides of 50 amino acid residues in length or longer, nor of 19-49 amino acid residues in length that possess the attributes recited in the instant claims, i.e., is specifically recognized by RA autoimmune antibodies from patients suffering from RA and that possess the recited motifs of the instant claims.

Indeed, the specification discloses that SEQ ID NO: 14 (IGP1676) which is 14 amino acid residues in length which fits into the motif of SEQ ID NO: 6) was only reactive with 2 out of 159 RA sera, that the three-dimensional structure was disrupted from the parent peptide SEQ ID NO: 12 (IPG 1650, 18 amino acid residues in length) (page 33 at lines 13-18).

The specification further discloses the criteria essential for accomplishing a three-dimensional structure and immunoreactivity with autoantibodies present in sera from RA patients (paragraph spanning pages 15 and 16 and continuing on pages 16 and 17) in type I peptides which have 6 amino acid residues between Cys residues, and those criteria essential in type II peptides which have 4 amino acid residues between Cys residues (lines 11-25 on page 17 and page 18 and page 19 at lines 1-5). However, the specification discloses these criteria only for peptides that are up to and including 18 amino acid residues in length, and includes possible amino acid substitutions at various positions in the peptides.

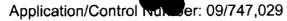
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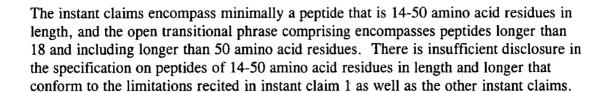


One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

8. Claims 1-9, 12-15, 18, 20 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how to make/and or use the claimed peptide comprising a sequence of 14-50 amino acids or longer, nor of 18 amino acid residues or longer, nor how to use the claimed peptide comprising SEQ ID NO: 4 or SEQ ID NO: 12, composition thereof and immunotoxin or kits comprising the said peptide for diagnosis of rheumatoid arthritis. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass peptides that are longer than 18 amino acid residues and that are not specifically recognized by autoimmune antibodies from patients suffering from rheumatoid arthritis (RA).





The specification discloses peptides of less than 50 amino acids that contain a peptide turn comprising at least one citrulline residue, less than 12 amino acid residues between two cysteine residues with said citrulline residue being one of the amino acids between the said cysteine residues and the said peptide being specifically recognized by autoimmune antibodies from patients suffering from RA (page 5 at lines 13-19). The specification discloses that the peptides have a length of preferably 40, 30, 25, 20 or less amino acids (page 7 at lines 23-26). The specification further discloses that the said peptides have a length between 13 and 19 amino acids (page 10 at lines 9-11). The specification discloses peptides with motifs 18 amino acids or less in length recited in instant claim 7, and peptides with complete sequences of 18 amino acids or less in length recited in instant claim 9.

The specification does not disclose peptides of 50 amino acid residues in length, nor of 19-49 amino acid residues in length that possess the attributes recited in instant claim 1, i.e., is specifically recognized by RA autoimmune antibodies from patients suffering from RA and that possess the recited motifs of the instant claims.

Indeed, the specification discloses that SEQ ID NO: 14 (IGP1676) which is 14 amino acid residues in length which fits into the motif of SEQ ID NO: 6) was only reactive with 2 out of 159 RA sera, that the three-dimensional structure was disrupted from the parent peptide SEQ ID NO: 12 (IPG 1650, 18 amino acid residues in length) (page 33 at lines 13-18).

The specification further discloses the criteria essential for accomplishing a three-dimensional structure and immunoreactivity with autoantibodies present in sera from RA patients (paragraph spanning pages 15 and 16 and continuing on pages 16 and 17) in type I peptides which have 6 amino acid residues between Cys residues, and those criteria essential in type II peptides which have 4 amino acid residues between Cys residues (lines 11-25 on page 17 and page 18 and page 19 at lines 1-5). However, the specification discloses these criteria only for peptides that are up to and including 18 amino acid residues in length, and includes possible amino acid substitutions at various positions in the peptides.

The specification discloses (on page 2 at line 24-31 and continuing on to page 3 at lines 1-3) that serological support for diagnosing RA is not very well established and is based mainly on the presence of rheumatoid factors (RF), that a number of RA patients are RF negative while RF is also found in a variety of other rheumatic diseases. The specification further discloses (on page 13 at lines 12-30 and page 14 at line 31) that a

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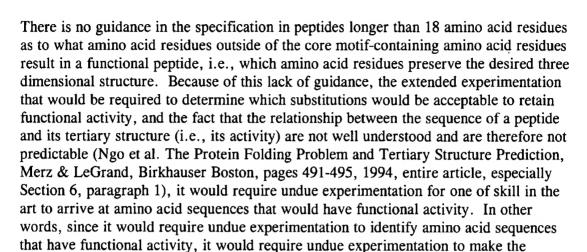
set of citrullinated peptides generated using molecular modeling and computational chemistry which are reactive with the autoimmune antibodies have a similar three-dimensional structure comprising a peptide turn. The specification discloses testing a number of previously diagnosed (on the basis of ACR criteria) RA patients' sera for reactivity with multiple citrullinated peptides of the invention (on page 35-41). The specification discloses a high specificity for reactivity of the peptides with the RA sera and complementarity with the RF test. The specification does not disclose treating rheumatoid arthritis or any other autoimmune disease in a subject animal, nor diagnosing patients with rheumatoid arthritis or any other autoimmune disease.

Evidentiary reference Jaarsveld et al (Clin Exp Rheum 1999, 17: 689-697, IDS reference) teaches that the CCP-ELISA (CCP, a cyclic citrullinated peptide) detects antibodies which recognize a subset of antiperinuclear factor and AKA (APF, profilaggrin, a potential prognostic marker for RA) determinants and that the reactivity of RA sera to different citrullinated peptide variants is highly diverse (especially page 695 at columns 1 and 2). Jaarsveld et al further teach that testing for APF by indirect immunofluorescence and the CCP-peptide ELISA assay together may have prognostic value to predict mild rheumatoid arthritis disease, but that reliable identification at baseline of individual patients with progressive disease is still not possible (especially Abstract). Jaarsveld et al also teaches that rheumatoid arthritis patients are a heterogeneous population (especially page 695 and 696); for example with respect to radiological damage scores the combination of RF and APF is a better prognostic marker than the single tests alone (especially page 696 at column 1, first paragraph). Evidentiary reference Schellekens et al (Arthritis & Rheum, 2000, 43(1): 155-163, IDS reference) teaches that although the anti-CCP ELISA assay is highly specific for rheumatoid arthritis, that further studies are clearly needed to substantiate the prognostic values of the anti-CCP assay, and that combining the anti-CCP assay with the IgM-RF ELISA increased the positive predictive value (especially page 162 at the last column).

Evidentiary reference Schellekens et al teaches that the anti-CCP ELISA was specific for established RA sera and moderately sensitive, and combined with the IgM-RF ELISA resulted in a higher positive predictive value, than using the IgM-RF ELISA alone (especially abstract). Schellekens et al further teaches peptide cfc1-cyc which is identical to peptide 1546 (SEQ ID NO: 22) of the instant specification, with one additional amino acid residue at the amino terminus, and which does not have less than 12 amino acid residues between cys residues. The instant specification discloses that peptide 1546 was comparable in sensitivity to the peptides 1611, 1646, 1650 and 1651 (table 7) which were cited by Applicant as superior in the amendment filed 12/2/02. Accordingly, there is a high level of unpredictability in diagnosing subjects with autoimmune diseases including rheumatoid arthritis using the claimed citrullinated peptides and Applicant does not provide direction or guidance to do so.

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corresponding sequences.



Accordingly, there is a high level of unpredictability in making and/or using the claimed citrullinated peptides and Applicant does not provide direction or guidance to do so. There is insufficient guidance in the specification as to how use the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments in the amendment filed 12/2/02 have been fully considered but are not persuasive.

Applicant's arguments are of record in section II of the said amendment. Briefly, it is Applicant's position that there is a need for diagnostic tools which make a very sensitive diagnosis of RA at high specificity level possible, that the features of the peptides as claimed in claim 1 include at least one citrulline residue, two cys residues separated by less than 12 amino acid residues with the citrulline residue, which is part of the peptide turn, and the peptide must be specifically recognized by RA antibodies. It is Applicant's further position that the peptides can be used for a more sensitive diagnosis than previously known peptides and cites Examples 3 and 4 of the instant specification. Applicant also cites IDS references filed 12/2/02 for support.

The Examiner maintains the arguments of record with regard to evidentiary reference Jaarsveld et al. In addition, it is the Examiner's position that evidentiary reference Schellekens et al teaches that the anti-CCP ELISA was specific for established RA sera and moderately sensitive using peptide cfc1-cyc which is identical to peptide 1546 (SEQ ID NO: 22) of the instant specification, with one additional amino acid residue at the amino terminus, and which does not have less than 12 amino acid residues between cys residues. The instant specification discloses that peptide 1546 was comparable in sensitivity to the peptides 1611, 1646, 1650 and 1651 (table 7). With regard to the said IDS references, the references were published in 2002. Applicant's invention must be enabled at the time of filing.



- 9. The following is a quotation of the second paragraph of 35 U.S.C. 112: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
- 10. Claims 15 and 25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
- a. Claim 25 is indefinite in the recitation of "small volume" because it is not clear what the metes and bounds of the said limitation are.
- b. Claim 15 is indefinite in the recitation of "specific recognized" because it is not clear what is meant.

Applicant's argument's in the amendment filed 12/2/02 have been fully considered but are not persuasive.

It is Applicant's position that small is defined on page 14 at lines 20-24 of the specification, i.e., the amino acids do not interact with the citrulline side chain, and that the skilled artisan would know that a measure of an amino acids volume is SSA and gives examples for Gly, Ala and Ser.

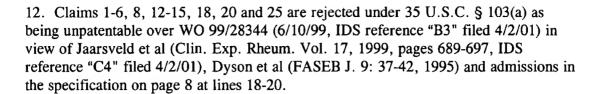
It is the Examiner's position that Applicant has disclosed Gly and Ser as having small volume, however, it is not disclosed what SSA is required to determine interaction with the citrulline side chain.

The following is a new ground of rejection.

- 11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103® and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

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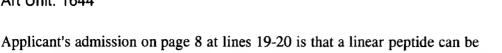
WO 99/28344 teaches circularized synthetic peptides (i.e., cyclic) containing less than 50 amino acid residues and containing at least one citrulline residue and which react with antibodies from patients with rheumatoid arthritis (RA). WO 99/28344 further teaches pharmaceutical compositions comprising the peptides for therapy or diagnosis, i.e., medicaments for treatment or a diagnosticum for rheumatoid arthritis or other autoimmune diseases, diagnostic kits, including wherein the peptides are attached to specific locations on solid substrate and combined with other peptide epitopes that can characterize autoimmune diseases or that are in solution for use as competitors, and immunotoxin molecules comprising the peptides, medicaments in which the peptide are in tandem repeats or branched forms to increase the size of the antigen-immune complexes to increase clearance and decrease immune complex deposition in the body, and the peptides in biotinylated form (entire document, especially abstract, pages 4-7, page 8 at lines 10-30 and continuing on to page 9 at lines 1-2 and 9-15, 23-31, page 10 t lines 1-8 and 21-31, page 11 at lines 1-31, Table 1 on page 13 and lines 25-31, page 20 at lines 1-25, page 23, page 26, claims). WO 9928344 teaches an overview of the amino acid substitutions that could form the basis of analogs of the peptides such as Cys for Ser, Thr or Met (especially Table 1 on page 13). WO 99/28344 teaches that the advantage of circularized forms of the said peptides was well known in the art and relates to an increased affinity of a conformationally constrained peptide as compared with the more randomly coiled forms of linear peptides (especially page 11 at lines 7-10).

WO 99/28344 does not teach that at least one citrulline residue is present in between two cysteine residues and that there are less than 12 amino acid residues between cysteine residues.

Jaarsveld et al teach an citrullinated cyclic peptide that was cyclized by substituting serine residues by cysterine (especially page 691, column 2 at the first full paragraph).

Dyson et al teach that immunogenic and antigenic peptides have been shown to have conformational preferences for structured forms, that the presence of structured forms is correlated with the location of T and B cell epitopes in peptide sequences, and frequently the bound peptides in complex with anti-peptide antibodies show the peptides bound in β -turn conformations (especially abstract). Dyson et al further teach that one approach to the problem of peptide conformational variability is to restrict the available conformations by covalent cross-linking of the peptide via cyclization (especially paragraph spanning columns 1 and 2 on page 40).

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circularized by any known method in the art, for example by the formation of a disulfide bond between two cysteine residues.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have substituted cysteine for serine in a peptide taught by WO 99/28344 such as the peptides in claim 3 as taught by WO 99/28344 and to produce a cyclic peptide as taught by Jaarsveld et al, WO 99/28344 and Dyson et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to cyclize the peptide as taught by Jaarsveld and Dyson et al and as per Applicant's said admission in the specification, and because WO 9928344 and Dyson et al teach the advantage of cyclizing the peptides for conformational stability. One of ordinary skill in the art at the time the invention was made would have been motivated to do this to prevent conformational dilution, i.e., to constrain the peptides to conformations that favor antibody binding in such a way that they can adopt the conformational features of the original antigenic site in the intact protein and in order to use lower amounts of the peptides.

Applicant's arguments in the amendment filed 12/2/02 have been fully considered, but are not persuasive.

It is Applicant's position on pages 13-15 of the said amendment that the references alone or in combination do not teach that the citrulline residue must occur within a peptide turn, that the combination does not suggest that the peptides could be used to aid in the diagnosis of RA, that cyclizing the peptides taught by WO 99/28344 would not produce the claimed invention.

It is the Examiner's position that WO 99/28344 teaches that the presence of the citrulline residue is crucial for reacting with antibodies that are present in sera from patients with RA (especially claims). It is the Examiner's further position that one of ordinary skill in the art at the time the invention was made would have been motivated to cyclize the peptides to prevent conformational dilution, i.e., to constrain the peptides to conformations that favor antibody binding in such a way that they can adopt the conformational features of the original antigenic site in the intact protein as taught by Dyson et al. WO 99/28344 teaches that the peptides react with antibodies that are present in sera from patients with RA, and further teaches that the peptides can be used for treatment and diagnosis of RA (especially claims and Abstract).

13. SEQ ID NO: 4 and 12 appear to be free of the prior art.

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14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is 703-308-0061. The examiner can normally be reached on Monday and Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Marianne DiBrino, Ph.D.

Patent Examiner

Group 1640

Technology Center 1600

July 24, 2003

CHRISTINA CHAN

PRVISORY PATENT EXAMINER